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Reply Brief
J. Bruce
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Attorney's Do. No. 4430-18

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Andrew D. Barofsky & Kenton W. Gregory

Serial No.: 08/797,770

Art Unit: 3738

Filed: February 7, 1997

Examiner: Paul Prebilic

For: METHOD FOR USING TROPOELASTIN AND FOR PRODUCING TROPOELASTIN BIOMATERIALS

Confirmation No. 1692

Mail Box Appeal Brief
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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TRANSMITTAL LETTER FOR APPELLANT'S REPLY BRIEF

This in response to the Examiner's Answer Brief, Confirmaton No. 1692 dated October 21, 2003.

This brief is in furtherance of the Notice of Appeal filed on November 5, 2002 and the Amended Appeal Brief filed on June 30, 2003. This is an appeal from the rejection, dated September 11, 2002, of claims 1-13, 15-24, 36-39, 41-55, 74 and 76-104 in the above-identified patent application. No fee for filing this Reply Brief in support of the appeal under 37 CFR 1.17(f) is due.

Applicant believes that no further extension of time is required, however if applicant has inadvertently overlooked the need for a petition and fee for extension of time, the Commissioner is authorized to charge any fees due to deposit account number 13-1703.

This Reply Brief is submitted in triplicate.

Customer Number 20575

Respectfully submitted,

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APPELLANT'S REPLY BRIEF UNDER 37 CFR 1.193(b)(1)

This brief contains these items under the following headings and in the order set forth below (37 CFR 1.192(c):

TABLE OF CONTENTS

I. INTRODUCTION

In response to the Examiner's Answer Brief, Confirmation No. 1692, dated October 21, 2003:

This brief is in furtherance of the Notice of Appeal filed on November 5, 2002 and the Amended Appeal Brief filed on June 30, 2003. This is an appeal from the rejection, dated September 11, 2002, of claims 1-13, 15-24, 36-39, 41-55, 74 and 76-104 in the above-identified patent application. No fee for filing this Reply Brief in support of the appeal under 37 CFR 1.17(f) is due. This Reply Brief is submitted in triplicate.

II. STATUS OF CLAIMS-37 CFR §1.192(c) (1)

A. Claims in the application are: 1-13, 15-24, 36-39, 41-55, 74 and 76-100 and 103-104.

B. Status of All the Claims is as detailed in the Examiner's Answer Brief.

III. STATUS OF AMENDMENTS-37 CFR §1.192(c) (2)

The Status of Amendments is unchanged from the Status submitted in Appellant's Amended Brief. The Examiner agrees with the correctness of this Status.

IV. SUMMARY OF THE INVENTION-37 CFR §1.192(c) (3)

The Summary of the Invention is unchanged from the Summary submitted in Appellant's Amended Brief. The Examiner agrees with the correctness of this Summary.

V. ISSUES ON APPEAL-37 CFR §1.192(c) (4)

A. First Issue: Withdrawn by the Examiner.

B. Second Issue: Whether claims 1-13, 15-24, 36-39, 41-55, 74 and 76-100 and 103-104 are unpatentable under 35 U.S.C. § 102(a) as anticipated by WO 96/14807 to Gregory et al ("Gregory, et al").

C. Third Issue: Whether claims 1-13, 15-24, 36-39, 41-55, 74 and 76-100 and 103-104 are unpatentable under 35 U.S.C. § 103(a) as obvious over Gregory et al in view of U.S. Patent No. 5,428,014 to Labroo et al ("Labroo et al ").

D. Fourth Issue: Whether claim 47 is unpatentable under 35 U.S.C. § 102(b) as being anticipated by Bedell-Hogan et al. in the JOURNAL OF BIOLOGICAL CHEMISTRY, page 1, lines 120-23 ("Bedell-Hogan et al ").

E. Fifth Issue: Withdrawn by the Examiner.

VI. GROUPING OF CLAIMS-37 CFR §1.192(c) (5)

The Examiner states that the claims stand or fall together with the particular rejections they are associated. Appellant notes that two grouped claim sets (Groups 2 and 5) previously stood rejected under 35 U.S.C. § 102(a). The Examiner has withdrawn the rejection of Group 5 claims without affecting Group 2, despite the Groups' having shared a common statutory basis for rejection (35 U.S.C. § 102(a)).

VII. ARGUMENTS-37 CFR §1.192(c) (6)

A. Rejections Under 35 U.S.C. § 112, second paragraph, of Group 1 Claims

Issue: Withdrawn by the Examiner.

B. Rejections Under 35 U.S.C. §102 of Group 2 Claims

Issue: Whether claims 1-13, 15-24, 36-39, 41-55, 74 and 76-100 and 103-104 are unpatentable under 35 U.S.C. § 102(a) as anticipated by Gregory et al. (See Examiner's Action, September 11, 2002, p. 3-4; Answer Brief, p. 4-5.)

1. The Interpretation of the Claims Has Changed

The Examiner has withdrawn the previous rejection under 35 U.S.C. § 112 ¶ 2. This rejection formerly had resulted in the Examiner's construction of "consisting essentially of tropoelastin" to be as broad as "comprising tropoelastin". The Examiner cited and applied prior art to the claims as he previously had broadly construed them.

As a result of the § 112 ¶ 2 rejection withdrawal, the proper scope of the pending claims has narrowed to the proper meaning of "consisting essentially of", a claim construction urged throughout prosecution by Appellant. The Examiner and the Board must view the rejections and asserted art in the context of the claims as they currently stand, including the proper construction of this transitional phrase to which the Examiner has acquiesced.

2. The Cited Art Does Not Teach a Biomaterial Consisting Essentially of Tropoelastin

The Examiner posits that "tropoelastin is so similar to elastin in tissue binding properties that it is considered interchangeable therewith" and obvious to use in the composition of the Gregory et al. reference. (See Examiner's Answer, p. 4 (citing Labroo, column 9, lines 1-26).) Such interchangeability is not taught by Labroo or Gregory et al.

Assuming, in arguendo, that elastin and tropoelastin could be interchanged, the fact remains that Gregory et al. teaches a heteropolymer comprising, among other things, fibrinogen or cryoglobulins, collagen, thrombin, and potentially a protease inhibitor. (See Gregory et al., p. 8-9.) The homopolymeric biomaterial of the rejected claims is patentably distinct from the heteropolymeric composition of Gregory et al. The substitution of tropoelastin for solubilized elastin–a suggestion not found in Gregory et al.–also does not result in the claimed invention.

3. "Tropoelastin" and "Elastin" Are Not Interchangeable Terms

The Examiner urges the Board to accept incorrect linguistic positions critical to the rejections. Specifically, the Examiner asserts that "tropoelastin" be equated with "elastin" and any biomaterial comprising tropoelastin equated with "elastin". Appellant traverses these linguistic errors.

First, the Examiner asserts that "tropoelastin is elastin even though it is not called such in the disclosure because the tropoelastin is uncrosslinked and unpolymerized precursor to elastin". (Examiner's Answer Brief, p. 4.) The Examiner supports this construction with the Gregory reference's mention of soluble elastin (page 8, lines 20-21), inferring that such phrase means tropoelastin (naturally-occurring elastin is insoluble, while tropoelastin is soluble). In discussing "soluble elastin", the Gregory reference defines it by reference to Rabaud et al., JOURNAL OF BIOMATERIALS APPLICATIONS, 7:2046 (1992). Rabaud clearly teaches that its solubilized elastin

is a chemical and enzymatic tissue-harvested elastin degradate, (see Rabaud, p. 21-22) and not by the synthesis and collection of pure tropoelastin.

Second, the Examiner states that "tropoelastin" and "elastin" are interchangeable terms in the disclosure according to Labroo. To the contrary, Labroo offers elastin and tropoelastin as two distinct moieties, each employable as a second polypeptide monomer in that reference's claimed copolymer. (Labroo, column 9, lines 1-21.) The terms are not used in Labroo to denote a single moiety.

4. A Biomaterial "Consisting Essentially of Tropoelastin" is Not "Elastin-Based"

The Examiner states that the claimed biomaterial is "elastin or elastin-based" is made from tropoelastin. (Examiner's Answer Brief, p. 4.) Appellant cannot agree that any biomaterial containing tropoelastin is therefore "elastin or elastin-based" per se.

Elastin is a biological compound with known structure and physical properties. Naturally-occurring elastin displays a regular molecular structure, and its polymerization in vivo is accomplished via specific enzymes and at specific sites on the tropoelastin and other building blocks. By contrast, tropoelastin is a polypeptide used as a building block, in combination with other moieties, in the in vivo synthesis of elastin.

Appellant's artificially-crosslinked biomaterial is recited as "consisting essentially of [crosslinked] tropoelastin", does possess the same polymeric structure or physical properties as elastin, and is not derived from elastin. The biomaterial of the present claims consists essentially of tropoelastin, randomly crosslinked in vitro by a crosslinking agent–o ordered crosslinking scheme exists in the claimed biomaterial. Neither Gregory nor Labroo support the Examiner's position, as purported by the Examiner.

It is further asserted that "when tropoelastin is formed into a biomaterial by crosslinking or polymerization, it becomes elastin." (Id.) This statement is technically true, in that naturally-occurring elastin does indeed comprise crosslinked tropoelastin. However, the implied proposition that whenever tropoelastin is formed into a biomaterial by crosslinking or polymerization, it becomes elastin is factually incorrect. Any assertion that the claimed biomaterial–randomly crosslinked and consisting essentially of tropoelastin–is structurally identical to elastin–a naturally occurring, biologically produced compound comprising a plurality of moieties–is also factually incorrect.

5. The Maslen Declaration

The Examiner asserts for the first time in his Answer Brief that the Maslen Declaration fails to meet any of the four requirements for filing a declaration under 37 C.F.R. § 1.131. (See Examiner's Answer, p. 5.) The Maslen Declaration was first presented to the Examiner during prosecution on June 24, 2002. No objection was lodged by the Examiner during prosecution, when Appellant would have had an opportunity to address and correct the Maslen Declaration.

The Examiner dismisses the Maslen Declaration as failing to demonstrate that the claimed method was performed at any time. (See Examiner's Answer, p. 5.) It is believed that the Examiner misunderstands the relevance of the Maslen Declaration. This Declaration is submitted to serve as independent testimony evidence of diligence relating to the claimed invention, not as evidence of actual reduction to practice. To the extent that this Declaration was identified as being submitted under 37 C.F.R. § 1.131, Appellant regrets any confusion which may have occurred. However, the substance of the Maslen Declaration stands as submitted and must be considered by the Board in its proper evidentiary light.

6. The Gregory/Barofsky Declaration

The Examiner further faults the Gregory Declaration as having not been executed by all of the inventors. To the contrary, Declarations executed by each of the inventors were previously filed in this case, averring facts relevant to this rejection. (See Amendment, July 8, 1999.) Appellant believes that the Board has before it the necessary facts presented by all inventors of the herein, despite the fact that such averments are housed in a plurality of Declarations.

7. Research on an Invention Closely Related to the Invention of the Claims

The Board and the Federal Circuit both have recognized the possibility that research might proceed on an invention closely related to the invention of the claims, and both bodies have held that an inventor should, in some circumstances, be able to rely on such closely-related work as support for establishing diligence toward Appellant's constructive reduction to practice of the claimed invention. See Ginos v. Nedelec, 220 USPQ 831, 835-36 (BPAI 1983); Hoffman v. Schoenwald, 15 USPQ2d 1512, 1515 (Fed. Cir. 1990) (graduate student's work in preparing compounds outside claims viewed as diligence activity).

In Ginos, Applicant's evidence showed that he performed no work on compounds encompassed by the interference count. Ginos, 220 USPQ at 835. Nevertheless, the Board found work to have been continuously performed on the preparation of other compounds considered by the inventor to be part of the same invention. Id. The Board expressly held that Ginos' work on the closely-related compounds during the critical period was "sufficiently related to his work on the invention in issue to count as diligence toward the reduction to practice of this invention." Id. at 836.

In the instant case, the inventors sought an in vitro expression system for the production of a recombinant tropoelastin monomer. The expression system was intended to provide tropoelastin monomer for their continued research regarding the invention encompassed by the claims. (Gregory Decl., ¶ 3, 6-7.) Because the inventors' laboratory does not routinely engage in expression system research and development, the inventors collaborated with Dr. Cheryl Maslen to develop the expression system for the use and benefit of the inventors herein. (Id., ¶ 3-7; Maslen Decl., ¶ 3-7.)

The independent testimony evidence of Dr. Maslen states:

- Dr. Maslen conducted tropoelastin research at OHSU in collaboration with the inventors.
- The tropoelastin research conducted by Dr. Maslen was funded entirely by Inventor Gregory.
- Dr. Maslen's work on tropoelastin began on or about September 1995, with the direct participation of inventor Barofsky, and was undertaken by Mr. Barofsky, Dr. Maslen, and her laboratory personnel and students.
- The tropoelastin research was performed by Dr. Maslen substantially continuously from September 1996 to at least February 7, 1997.
- Dr. Maslen's tropoelastin research has continued to past the date of execution of Dr. Maslen's Declaration, without having been halted or abandoned for other research projects, lack of funding or personnel, or other administrative or financial reasons.
- Inventor Gregory has supervised the tropoelastin research in Dr. Maslen's laboratory, and Dr. Maslen has made regular progress reports to Inventor Gregory regarding the tropoelastin research.
- Dr. Maslen's regular progress reports have been included in reports made by Inventor Gregory to his research grant sponsor.

As discussed supra, the Federal Circuit has approved similar secondary activities as evidencing diligence in reducing to practice the claimed invention. The work of Dr. Maslen on the closely-related tropoelastin expression system–intended to provide the inventors with

tropoelastin monomer for their research of tropoelastin polymers and begun prior to the start of the critical period and extending later in time than Applicants' filing date–therefore is proper evidence of Applicants' diligence during the critical period.

C. Rejections Under 35 U.S.C. §103 of Group 3 Claims

Issue: Whether claims 1-13, 15-24, 36-39, 41-55, 74 and 76-100, and 103-104 are unpatentable under 35 U.S.C. § 103(a) as obvious over Gregory et al in view of U.S. Patent No. 5,428,014 to Labroo et al. (See Examiner's Action, September 11, 2002, p. 5.)

1. The Interpretation of the Claims Has Changed

Appellant reiterates its argument that withdrawal of the § 112 ¶ 2 has altered the Examiner's claim interpretation to the proper meaning of "consisting essentially of". The § 102(a) rejection and asserted art must give proper deference to the "consisting essentially of" transitional phrase.

2. The Cited Art Does Not Teach a Biomaterial Consisting Essentially of Tropoelastin

Gregory et al. teaches a heteropolymer comprising, among other things, fibrinogen or cryoglobulins, collagen, thrombin, and potentially a protease inhibitor. (See Gregory et al., p. 8-9.) The homopolymeric biomaterial of the rejected claims is patentably distinct from the heteropolymeric composition of Gregory et al. The substitution of tropoelastin for solubilized elastin–a suggestion not found in Gregory et al.–also does not result in the claimed invention.

Labroo discusses both homopolymers and copolymers. It is only in the context of a copolymer that Labroo suggests use of elastin or tropoelastin–i.e., as one component in a plurality of components used to form a heteropolymeric construct. Labroo does not contemplate the use of elastin or tropoelastin in a homopolymeric compound. Critically, Labroo further fails to discuss a biomaterial "consisting essentially of" tropoelastin.

Even assuming Gregory is prior art to the present application, the combination of Gregory et al. and Labroo nevertheless does not teach or fairly suggest a biomaterial consisting essentially of tropoelastin. Labroo is the only reference that in any way addresses a homopolymer. But Labroo, while knowledgeable of elastin and tropoelastin, suggests the use of these moieties for a

heteropolymer but not for a homopolymer. To the extent that Labroo teaches anything of homopolymers consisting essentially of a moiety, Labroo teaches away from using tropoelastin or elastin in such a homopolymer. Gregory et al. does not counter this Labroo teaching.

3. "Tropoelastin" and "Elastin" Are Not Interchangeable Terms

To support the § 103(a) rejection, the Examiner urges the Board to accept linguistic positions critical to the rejections, which linguistic errors Appellant has traversed supra (Section VII.B.3-4). The assertion that a biomaterial comprising tropoelastin equated with elastin is especially ill-founded given the Examiner's acquiescence that "consisting essentially of" is no longer interpreted to mean "comprising".

D. Rejections Under 35 U.S.C. §102 of Group 4 Claim

Issue: Whether claims 47 is unpatentable under 35 U.S.C. § 102(b) as being anticipated by Appellant's "admission or description" of Bedell-Hogan et al. in the JOURNAL OF BIOLOGICAL CHEMISTRY, page 1, lines 120-23 ("Bedell-Hogan"). (See Examiner's Action, September 11, 2002, p. 5. (withdrawing this rejection as to claim 48))

Claim 47 has been rejected under 35 U.S.C. § 102 (b) as being anticipated not by Bedell-Hogan, but by Applicants' characterization of the teaching of Bedell-Hogan. (See Office Action, September 11, 2002, p. 5 ("anticipated by Applicants' Admission wherein the claimed process of tropoelastin polymerization reads on the natural process of elastin formation in vertebrates according to Bedell-Hogan"); Examiner's Answer, p. 8.)

Anticipation under 35 U.S.C. § 102 (b) requires that every element of the claim be found in the prior art reference. The method of claim 47 is not described in Appellant's "admission" as to the Bedell-Hogan reference. In the Background of the Invention, Appellant stated:

> The most abundant component of elastic fibers is elastin. The entropy of relaxation of elastin is responsible for the rubber-like elasticity of elastic fibers. In vertebrates elastin is formed through the secretion and crosslinking of tropoelastin, the 72-kDa biosynthetic precursor to elastin. This is discussed, for example, in an article entitled "Oxidation, Cross-linking, and Insolubilization of Recombinant Crosslinked Tropoelastin by Purified Lysyl Oxidase" by Bedell-Hogan, et al in the Journal of Biological Chemistry, Vol. 268, No. 14, on pages 10345-10350 (1993).

It is clear that Applicants' characterization of the process of elastin in vivo synthesis as "the secretion and crosslinking of tropoelastin" is generic; the reader is expressly directed to the Bedell-Hogan article for a more detailed discussion of elastin in vivo synthesis.

The citation to Bedell-Hogan is flanked by paragraphs discussing in vivo tissues and repairs, clearly meaning that the reference is directed to in vivo elastin synthesis. Moreover, to the extent that the teaching of Bedell-Hogan is incorporated implicitly by reference, the cited reference directly contradicts the Examiner's asserted "admission". The Bedell-Hogan article itself describes the "other macromolecules which may be involved in this process [of polymerization of tropoelastin into elastin fibrils] in vivo." (See Bedell-Hogan, p. 10349.)

By contrast, the crosslinking disclosed in the present application utilizes a nonspecific, random chemical crosslinking agent to produce a polytropoelastin biomaterial in vitro. The biomaterial of claim 47 consists essentially of tropoelastin. Naturally-occurring elastin (a hetero- or co-polymer) and the biomaterial of claim 47 (a homopolymer) are structurally and patentably distinct compositions of matter.

The generic characterization of Bedell-Hogan, taken in combination with the teachings of Bedell-Hogan itself, contradicts and does not support the "Applicants' Admission" conclusion advanced by the Examiner. Therefore, the above rejection does not constitute prima facie anticipation under 35 U.S.C. § 102 (b).

E. Rejections Under 35 U.S.C. §102 of Group 5 Claims

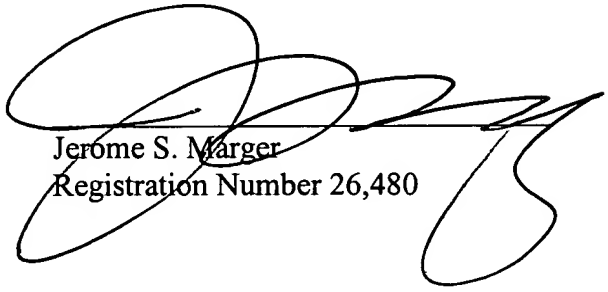
Issue: Withdrawn by the Examiner.

VIII. APPENDIX 37 CFR§1.192(c) (7)

The text of the claims on appeal are claims 1-13, 15-24, 36-39, 41-55, 74 and 76-104, which remain unchanged from Appellant's initial Appeal Brief.

Customer Number 20575

Respectfully submitted,



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